

What is claimed is:

1. A potassium channel comprising four hydrophobic domains capable of forming transmembrane helices, wherein
 - (i) a first pore-forming domain is interposed between a first and a second transmembrane helix; and
 - (ii) a second pore-forming domain is interposed between a third and a fourth transmembrane helix.
2. The potassium channel of Claim 1 wherein each pore-forming domain comprises a potassium selective peptide motif selected from the group consisting of dipeptide motifs and tripeptide motifs.
3. The potassium channel of Claim 2 wherein the peptide motif comprises GXG wherein X is selected from the group of amino acids V, L, Y, F, M, or I.
4. The potassium channel of Claim 3 wherein the pore-forming domain comprises $ZXXZ_1Z_2Z_4GXG$ wherein
 - (i) Z through Z_2 are amino acid residues comprising T or S;
 - (ii) Z_3 is an amino acid residue comprising I or V; and
 - (iii) X is an amino acid residue comprising V, L, Y, F, M, or I.
5. The potassium channel of Claim 4 where X is L or I.
6. The potassium channel of Claims 1, 2, 3, 4, or 5 wherein at least one pore-forming domain is positioned proximal to an exterior portion of a cell membrane.

7. The potassium channel of Claim 5 further comprising an amino acid motif $ZX_1X_2X_3GX_4PX_5$ downstream of said first pore-forming domain.

8. The potassium channel of Claim 7 wherein $ZX_1X_2X_3GX_4PX_5$ is positioned about 12-25 amino acids downstream of said first pore-forming domain.

9. The potassium channel of Claim 8 wherein $ZX_1X_2X_3GX_4PX_5$ is positioned within the second transmembrane domain.

10. The potassium channel of Claim 8 or 9 wherein $ZX_1X_2X_3GX_4PX_5$ is positioned beginning about 16 amino acids downstream of said first pore-forming domain.

11. The potassium channel of Claim 8, 9 or 10 wherein a second $ZX_1X_2X_3GX_4PX_5$ peptide is located within said second pore-forming region.

12. The potassium channel of Claim 8, 9, or 10 wherein $ZX_1X_2X_3$ comprises the amino acids YALL.

13. The potassium channels of Claim 12 wherein $ZX_1X_2X_3GX_4P$ comprises the amino acids YALLGIP.

14. The potassium channel of Claim 4 further comprising a glycosylation site.

15. The potassium channel of Claim 14 wherein said glycosylation site is asparagine-linked.

Sub E4
16. The potassium channel of Claims 1, 2, 3, 4, 5, 7, or 8 characterized in that it is derived from invertebrates.

17. The potassium channel of Claim 16 characterized in that it is insect-derived.

18. The potassium channel of Claim 16 characterized in that it is nematode-derived.

Sub E5
19. The potassium channel of Claims 1, 2, 3, 4, 5, 6, 7, or 8 characterized in that it is derived from vertebrates.

20. The potassium channel of Claim 19 characterized in that it is mammalian derived.

21. The potassium channel of Claim 20 characterized in that it is human derived.

Sub J1
22. An isolated nucleotide sequence capable of encoding a protein designated CORK.

23. An isolated nucleotide sequence capable of encoding a protein designated hORK.

08816011.031197
/611EO" TT091880

Sub
E6

24. An isolated nucleotide sequence comprising
- (i) a nucleotide sequence depicted in SEQ ID NO 1 or 36;
 - (ii) a nucleotide sequence that hybridizes to said sequence depicted in SEQ ID NO:1 or 36;
 - (iii) a nucleotide sequence that is degenerate to the nucleotide sequence depicted in SEQ ID NO:1 or 36; and
 - (iv) a functional derivative of the nucleotide sequence depicted in SEQ ID NO:1 or 36.
25. An isolated nucleotide sequence comprising
- (i) a nucleotide sequence depicted in SEQ ID NO:46;
 - (ii) a nucleotide sequence that hybridizes to said sequence depicted in SEQ ID NO:46;
 - (iii) a nucleotide sequence that is degenerate to the nucleotide sequence depicted in SEQ ID NO:46; and
 - (iv) a functional derivative of the nucleotide sequence depicted in SEQ ID NO:46.
26. An isolated nucleotide sequence comprising
- (i) a nucleotide sequence depicted in SEQ ID NO:51, 52 or 53;
 - (ii) a nucleotide sequence that hybridizes to said sequence depicted in SEQ ID NO:51, 52 or 53;
 - (iii) a nucleotide sequence that is degenerate to the nucleotide sequence depicted in SEQ ID NO:51, 52 or 53; and
 - (iv) a functional derivative of the nucleotide sequence depicted in SEQ ID NO:52, 52, or 53.

27. An expression vector capable of expressing the potassium channel of Claim 16 in a cell membrane of a yeast cell.

28. An expression vector capable of expressing the potassium channel of Claim 19 in a cell membrane of a yeast cell.

29. An expression vector capable of expressing the potassium channel encoded by the nucleotide sequence of Claims 24, 25, or 26 in a cell membrane of a yeast cell.

30. A transformed yeast cell comprising the expression vector of Claims 27, 28, or 29.

31. A method of assaying substances to determine effects on cell growth, the method comprising the steps of:

- a) preparing cultures of yeast cells in a medium adequate to support growth of potassium-dependent mutant strains expressing the potassium channel of Claim 1;
- b) contacting said substance to a portion of said yeast cells thereafter permitting sufficient time for continued growth, if any, of the portion of yeast cells so contacted as well as the portion not contacted with said substance;
- c) identifying zones of growth around the substances, wherein the level of growth indicates whether or not activity of the

heterologous potassium channel has been modulated as compared to yeast cells not contacted with said substances.

32. The method of Claim 31 wherein said yeast cells comprise the nucleotide sequence of Claims 24, 25, or 26.

33. A kit comprising the nucleotide sequences of Claim 32.

34. A method of modulating the activity of the potassium channel of Claim 19, positioned in a cellular membrane of a living organism by contacting said cellular membrane with a substance, in an amount and for a period of time sufficient to modify the ability of potassium ions to pass through said channel positioned in said cellular membrane of the living organism.

35. A method of modulating cardiac activity, by applying to a patient in need of such cardiac modulation, a substance capable of interacting with a potassium channel contained in the cardiac cells of such patient that is biologically equivalent to the potassium channel encoded by SEQ ID NO:1 or 46, and modulating the activity of same.

36. The potassium channel of Claim 7 capable of rectifying the inward and outward flow of ions.

37. The potassium channel of Claim 7 capable of rectifying the outward flow of ions.

38. The potassium channel of Claim 36 or 37 wherein direction and magnitude of potassium current is modulated by external potassium in concentration.

39. The potassium channel of Claim 36 or 37 wherein potassium is the permeant ion.

40. A method of chromosome mapping comprising

(i) providing PCR primers from the nucleotide sequence of Claims 24, 25, or 26;

(ii) performing a PCR assay of somatic cell hybrids containing chromosomes using the primers of step i); and

(iii) detecting amplified fragments as a measure of the hybrids containing the gene corresponding to the primers.

41. A transgenic animal comprising the nucleotide sequence of Claims 24, 25, or 26.